

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

To:

see form PCT/ISA/220

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/US2005/006627

International filing date (day/month/year)
24.02.2005

Priority date (day/month/year)
25.02.2004

International Patent Classification (IPC) or both national classification and IPC
C07D491/04, A61K31/436, A61P29/00

Applicant
LIGAND PHARMACEUTICALS INCORPORATED

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



European Patent Office - P.B. 5818 Patentlaan 2
NL-2280 HV Rijswijk - Pays Bas
Tel. +31 70 340 - 2040 Tx: 31 651 epo nl
Fax: +31 70 340 - 3016

Authorized Officer

Diederer, J

Telephone No. +31 70 340-1097



**WRITTEN OPINION OF THE
 INTERNATIONAL SEARCHING AUTHORITY**

International application No.
 PCT/US2005/006627

Box No. 1 Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 - ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - ☐ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☐ in written format
 - ☐ in computer readable form
 - c. time of filing/furnishing:
 - ☐ contained in the international application as filed.
 - ☐ filed together with the international application in computer readable form.
 - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US2005/006627

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,
- ☒ claims Nos. 122-125

because:

- ☒ the said international application, or the said claims Nos. 122-125 (with respect to industrial application) relate to the following subject matter which does not require an international preliminary examination (*specify*):

see separate sheet

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☐ no international search report has been established for the whole application or for said claims Nos.
- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:
 - the written form ☐ has not been furnished
 - ☐ does not comply with the standard
 - the computer readable form ☐ has not been furnished
 - ☐ does not comply with the standard
- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.
- ☐ See separate sheet for further details

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US2005/006627

Box No. IV Lack of unity of invention

1. ☐ In response to the invitation (Form PCT/ISA/206) to pay additional fees, the applicant has:
- ☐ paid additional fees.
 - ☐ paid additional fees under protest.
 - ☐ not paid additional fees.
2. ☒ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is
- ☐ complied with
 - ☒ not complied with for the following reasons:
see separate sheet
4. Consequently, this report has been established in respect of the following parts of the international application:
- ☒ all parts.
 - ☐ the parts relating to claims Nos.

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	41-45, 84-86, 88-98, 100, 104, 105, 121
	No: Claims	1-40, 46-83, 87, 99, 101-103, 106-120, 122-137
Inventive step (IS)	Yes: Claims	
	No: Claims	1-137
Industrial applicability (IA)	Yes: Claims	1-121, 126-137
	No: Claims	

2. Citations and explanations

see separate sheet

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/US2005/006627

Re Item III.

Claims 122-125 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Re Item IV.

This Authority considers that there are two inventions covered by the claims indicated as follows:

- I: Claims 1-83 (in part), 99,100,106,107-137 (in part) directed to compounds of Formula (I) wherein R1 is an aromatic 6-membered ring (phenyl, naphthyl, pyridine)
- II: Claims 84-98, 101-105, 107-137 (in part) directed to compounds of Formula (I) wherein R1 is an unsaturated 5-membered heterocyclic ring (thienyl or oxalyl groups)

Reference is made to the following document:

D1: WO 02/02565 A (ABBOTT LABORATORIES; LIGAND
PHARMACEUTICALS INCORPORATED) 10 January 2002 (2002-01-10)

Document D1 discloses on page 36 and 37, compounds which are novelty destroying for claim 1 of the present application. These compounds are used for the same purpose as the compounds of the present application, i.e. modulation of glucocorticoid receptors. The compounds have either a pyridine or a phenyl groups corresponding with the R1 in the present application.

The only technical feature in claim 1 of the present application which can act as the special technical feature, as laid down on Rule 13.2 PCT, is the general Markush Formula (I). As this feature is not novel, and there are no other technical features which can act as special technical feature, there is a lack of Unity of Invention, according to Rule 13.2 PCT. The novelty destroying compounds as disclosed in D1 have in common that they all bear 6-membered aromatic rings as substituent like the corresponding R1 group of the present compounds. The application is therefore split into two parts, one in which R1 is an aromatic 6-membered ring and one wherein R1 is an unsaturated 5-membered heterocyclic ring.

Re Item V.

1. Novelty (Article 33(2) PCT)

The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 1-40, 46-83,87,99,101-103,106-120,122-137 is not new in the sense of Article 33(2) PCT.

Document D1 discloses on page 36 lines 20-23, 28-37 and page 37 line 1 several compounds which are used as modulators for glucocorticoid receptors. This disclosure is novelty destroying for claims 1-40, 46-83,87,99,101-103,106-120,122-137 of the present application.

2. Inventive Step (Article 33(3) PCT)

The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 1-137 does not involve an inventive step in the sense of Article 33(3) PCT.

In as far as the subject-matter of the present application is novel, it does not contain any additional features in the claims which, in combination with the claims they depend on, render the subject-matter inventive over the prior art.